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ORIGINAL ARTICLE

Influence of clinical and socioeconomic factors on the nutritional state of pediatric patients with cystic fibrosis

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Keywords:
cystic fibrosis, nutritional status, socioeconomic factors, epidemiology

Abstract

Objective: To verify the influence of clinical and socioeconomic factors on the nutritional status of pediatric CF patients treated at a referral care facility in the State of Piauí and to describe their general profile. **Methods:** This was an observational cross-sectional retrospective descriptive study with secondary data analysis, performed by data from medical records of 23 patients under 16 years of age with confirmed cystic fibrosis, attended at 2018, were collected. **Results:** There was a slight predominance of male and brown, homozygous (p=0.05), from southeast Piaui, in school age group. Age at diagnosis was 2.0±3.0 years, with 13% asymptomatic. Respiratory symptoms and growth deficits were the main initial manifestations. 47.8% were diagnosed by neonatal screening. Most had good and excellent score for the Shwachman-Kulczycki score, average of 78.5±16.7. Most were eutrophic, with adequate Z-score values. Influence of nutritional status on the Shwachman-Kulczycki score was noted, and the latter was found to be significantly lower (p=0.037) in patients with nutritional deficit. **Discussion:** There was a delay in the diagnosis of these patients, with low coverage of neonatal screening tests. The socioeconomic and clinical aspects did not influence the nutritional status, except for the severity score that was worse in those with nutritional deficit. **Conclusion:** Nutritional status influenced the severity score, confirming the importance of adequate management and nutritional monitoring for improving the quality of life.

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INTRODUCTION

Cystic Fibrosis (CF) or Mucoviscidosis is an autosomal recessive hereditary disease caused by alteration in a gene chain due to the absence or irregularity in the amount or expression of the Cystic Fibrosis Transmembrane Regulator (CFTR) protein. This acts in the stabilization of the chlorine ion in the membrane of the epidermal cells. In the lung, it generates an increase in mucus, culminating in respiratory dysfunction, bacterial proliferation and chronic infection; in pancreatic cells, obstruction of the ducts leads to enzymatic loss and difficulty in absorbing nutrients[1,2].

Many of the children are born asymptomatic, but the diagnosis can be made early by measuring Immunoreactive Trypsin (IRT), through the Neonatal Screening Test (NST)[3]. The main manifestations refer to respiratory infections associated with the chronic inflammatory process and malabsorption due to pancreatic failure. This triggers a secondary nutritional deficit, which also implies a worsening of pulmonary function[4]. Malnutrition is associated with a rapid progression of the lung disease, either by compromising the chest muscles and lung elasticity or by impairing the immune system[5].

According to the Brazilian Cystic Fibrosis Registry (REBRAFC) of the Brazilian Cystic Fibrosis Study Group (GBEFC)[6], between 2016 and 2017, 4,654 patients were identified with this disease in the country. The Northeast occupied the 3rd position with 17.2% of the patients. The United States, Canada and Europe have 1:2000 to 1:5000 cases among live births of Caucasian ethnicity, while in Brazil this number varies from 1:9000 to 9500[2]. In Piauí, in 2018, there were about 1:18,000 cases among live births[7].

Solomon, Bozec and Mascarenhas[8] stated that the adequate growth and development of these children need to be constantly monitored because of the risk of malnutrition, related to the inadequate balance between energy use and demand, chronic infections and reduced food intake. Thus, recognizing and monitoring nutritional and respiratory functions, in addition to clinical status. It is important to have adequate nutritional and drug support in order to avoid further complications. Estimating the nutritional losses of patients with CF is the main strategy to avoid complications[9,10].

The present study aimed to define the profile of pediatric patients with Cystic Fibrosis treated at a reference service in the State of Piauí, in relation to epidemiological, clinical and nutritional aspects. We had data on the diagnosis of the pathology and current clinical status of the individuals, anthropometric measurements and nutritional classification, in addition to socioeconomic aspects, aiming to promote a management directed towards the deficiencies and complications of these patients, with an increase in survival.

MATERIALS AND METHODS

We ran an observational, descriptive, retrospective study with a quantitative approach and secondary data analysis, in a Pediatric Hospital in the State of Piauí - a reference service for patients with CF. The population consisted of 23 pediatric patients followed up with confirmed CF according to the presence of at least one of the characteristic clinical manifestations and at least two measurements of chloride in sweat by iontophoresis with pilocarpine greater than 60mEq/L, or the presence of two known mutations for CF, through genetic study[9]. As this is a not-so-prevalent disease and, as a result, the population is small, the sample was for convenience and corresponded to all 23 individuals under 16 years of age, with confirmed CF, according to the criteria mentioned above, which attended consultations from January to December 2018.

Data collection took place from October to November 2019, through the analysis of medical records, respecting data confidentiality. The record was made in a structured form in order to obtain information regarding their socioeconomic conditions, clinical and nutritional characteristics.

Socioeconomic data included information on gender, age, skin color, origin, as well as maternal data regarding age, schooling and family income. The evaluation of clinical characteristics comprised data on the diagnosis of the pathology, such as neonatal screening, age and conditions present at diagnosis and genotyping. They also gathered information on medication use, pulmonary exacerbations, hospitalizations and the classification of disease severity through the Shwachman-Kulczycki[11] score during 2018.

The nutritional status of the patients was defined according to the anthropometric measurements of weight and height, performed during the last annual consultation. They were then classified based on the WHO Anthro and WHO Anthro Plus programs of the World Health Organization[12,13], obtaining Z-score values for weight for age (H/A); height for age (H/A); weight for height (W/H); in children under 5 years old, and body mass index (BMI) for age (BMI/I). Although the range between Z-scores -1 to -2 is classified as “Eutrophic”, according to the WHO[12,13], in this study, in order to define the presence of nutritional deficit, indices lower than Z-score -1 were considered, due to the important relationship between nutritional status and lung function prognosis, a criterion also adopted in other studies[14,15]. Percentile values were also obtained for nutritional classification since, according to the recommendations of Turck et al.[16], the goal of adequate nutritional status for these patients corresponds to W/H values, in children under 2 years old, and BMI/A, from 2 years old, greater than or equal to the 50th percentile.

We plotted the data on a Microsoft Office Excel 2019® spreadsheet and then transferred to the IBM SPSS Statistics® 21.0 statistical program and processed them into tables and graphs. Data were expressed as frequencies and percentages for qualitative variables and as measures of central tendency and dispersion for quantitative variables. Data normality was tested using the Shapiro-Wilk test for quantitative variables. After that, the t-Student test with a confidence interval of 95% was used for the variables that followed normality and

the Mann-Whitney test for the variables that did not follow normality. The association between categorical variables was tested using the Fisher's exact test, as some cells presented values lower than 5. Data were considered significant with P values below 0.05.

This study was carried out in accordance with Resolution No. 466/2012 of the Ministry of Health, with approval by the Research Ethics Committee of the Federal University of Piauí (CEP-UFPI), CAAE: 18722219.0.0000.5214.

RESULTS

Of the 23 CF patients followed at the service, all attended at least one consultation during the year 2018 and were included in the study. We found that 52.2% (n=12) were males and 47.8% (n=11) were females, with a median age of 3.8 years (interquartile range: 2.4 - 9, 6 years). Most individuals were brown (11/47.8%), coming from the southeastern region of Piauí (12/56.5%). Regarding maternal data, the average age of mothers was 31±7 years, with 12±4 years of schooling, with only 21.7% (n=5) of them having started or completed higher education, and 82,6% (n=19) had an income of 1-3 minimum wages.

The mean age of patients at diagnosis was 2.0±3.0 years, reaching a maximum age of 15 years. Only 13% of the patients were asymptomatic at diagnosis, with the most frequent clinical manifestations being persistent respiratory symptoms (16/69.5%) and growth deficits or malnutrition (15/65.2%) (Table 1).

Table 1. Clinical aspects of pediatric patients with cystic fibrosis followed up at a referral service in the state of Piauí in 2018. Teresina, 2019.

Clinical aspects	n	%
Signs and symptoms present upon diagnosis		
Growth deficit or malnutrition	15	65.2%
Steatorrhea or fecal evidence of malnutrition	11	47.8%
Metabolic disorder	5	21.7%
Persistent respiratory symptoms	16	69.5%
Family history	3	13.0%
Edema+anemia	3	13.0%
Asymptomatic	3	13.0%
Medication of continuous use		
Alpha-dornase	21	91.3%
Pancreatin	22	95.6%
Polyvitamins	21	91.3%
Vitamin E	12	52.1%
Levothyroxine	2	8.7%
Ursodesoxicholic acid	5	21.7%
Ferric compounds	11	47.8%
Folic acid	1	4.3%
Polyethylenoglycol	2	8.7%
Other	1	4.3%
None	0	0.0%
Shwachman-Kulczycki Score		
Severe	0	0.0%
Moderate	3	13.0%
Medium	4	17.4%
Good	9	39.1%
Excellent	7	30.4%

Legend: n, absolute frequency; %, relative frequency.

Only 11 individuals (47.8%) were diagnosed through NST. Regarding genotyping, there was a predominance of homozygous individuals (16/69.6%) (p=0.05). Throughout 2018, patients attended about 3.4±1.4 consultations and used an average of 4 continuous medications, being pancreatin (22/95.6%), alpha-dornase (21/91.3%) and multivitamins (21/91.3%) the main ones. 47.8% of the subjects (n=11) had pulmonary exacerbations during the year of follow-up and about 30.4% (n=7) required hospitalization. The assessment of the severity of the patients' current status was performed using the Shwachman-Kulczycki score[11], with a mean score of 78.5±16.7, with most patients classified as Good (9/39.1%) or Excellent (7/30.4%) (Table 1). There were no deaths during the annual follow-up.

The classification of nutritional status, based on the Z-score values of W/A, H/A and BMI/A[12,13], are contained in Table 2. It was evidenced that most individuals had adequate values of Z-score of W/A, H/A and BMI/A.

Table 2. Nutritional status of pediatric patients with cystic fibrosis followed up at a reference service in the state of Piauí, in 2018. Teresina, 2019.

Nutritional Score	n	%
BMI/A Z-Score:		
Obesity	0	0.0%
Overweight	0	0.0%
Risk of overweight	2	8.7%
Eutrophy	16	69.6
Leanness	4	17.4%
Extreme leanness	1	4.3%
E/I-Z Score		
Adequate	11	47.8%
Low	6	26.0%
Very low	6	26.0%
P/A-Z score		
High	0	0.0%
Adequate	12	52.1%
Low	6	26.0%
Very low	5	21.7%

Legend: n, absolute frequency; %, relative frequency.

About half of the patients (11/47.8%) used food supplements. Despite this, 16 patients had a nutritional deficit (Z-Score of W/A, W/H, H/A, BMI/A less than -1)[14,15]. There was statistical significance (p=0.03) between patients who reached and those who did not reach the nutritional recommendation suggested by Turck et al.[16]. It was observed that 82.6% (n=19) of the patients were out of nutritional recommendations, with only 17.4% (n=4) of patients reaching the nutritional status goal.

There was a nutritional status influence on the Shwachman-Kulczycki score[11], with the mean score in individuals with nutritional deficit significantly lower (*p*=0.037) than in those without such deficiency (Table 3).

Table 3. Presence of nutritional deficit and quantitative variables on socioeconomic and clinical aspects of pediatric patients with cystic fibrosis followed up at a reference service in the state of Piauí, in 2018. Teresina, 2019.

	Nutritional deficit		
	Yes[a]	No[b]	*p*-value
	Mean	Mean	
Socioeconomic characteristics			
Age (years)	5,6	6,7	NS*
Maternal age (years)	31	33	NS*
Maternal schooling	11	14	NS*
Clinical characteristics			
Age upon diagnosis (years)	1	2	NS**
Continuous-use medication	5	3	NS*
Number of pulmonary exacerbations	0,9	0,7	NS*
Number of consults	3,6	2,9	NS**
Number of hospital stays	0,6	0,1	NS**
Shwachman-Kulczycki score	73,8	89,3	0,037*

Legend: NS, No-significance; aZ-Score for P/I, P/E, E/I,BMI/A <-1; bZ-Scre P/I, P/E, E/I,BMI/A ≥ -1; *T-Student test; **Mann-Whitney test.

There was no statistical significance between poor nutritional status and socioeconomic characteristics, and the other clinical aspects evaluated (Tables 3 and 4).

Table 4. Nutritional deficit and qualitative variables on socioeconomic and clinical aspects of pediatric patients with cystic fibrosis followed up at a referral service in the state of Piauí, in 2018. Teresina, 2019.

	Nutritional Deficit				
	Yes[a]		No[b]		
	n	%	n	%	*p*-value
Sex					
Male	10	62.5%	2	28.6%	0.148
Female	6	37.5%	5	71.4%	
Neonatal screening diagnosis					
Yes	7	43.7%	4	57.1%	0.444
No	9	56.3%	3	42.9%	
Genetic testing					
Homozygotic	13	81.2%	3	42.9%	0.176
Heterozygotic	3	18.8%	3	42.9%	
Exacerbations pulmonary					
Yes	8	50.0%	3	42.9%	0.556
No	8	50.0%	4	57.1%	
Hospital stays					
Yes	6	37.5%	1	14.3%	0.275
No	10	62.5%	6	85.7%	
Total	16	100.0%	7	100.0%	

Legend: aZ-Score of H/A, H/E, H/A, BMI/A <-1; bZ-score of W/A, W/H, H/A, BMI/A ≥ -1; n, absolute frequency; %, relative frequency; Fisher's test.

DISCUSSION

The socioeconomic data on pediatric patients with CF in Piauí are similar to those found by the GBEFC[17], in the 2017 report, which found that 52% of the patients were males and 48% were females, with a predominance of white and brown individuals[5,18]. Children and adolescents aged up to 15 years corresponded to 59.2% of the total[17]. There is a peculiar characteristic concerning the origin of the cases, for more than half of the patients are from Southeast Piauí. Regarding maternal data, a study carried out in northeastern Brazil[14] showed similar data regarding age and maternal schooling of patients with CF. A higher level of maternal education enhances treatment compliance, causing an improvement in nutritional status. Family income could also influence clinical and nutritional status, as it favors access to healthcare services and medicines, but this study did not find significance between these variables. The adequate nutritional status found in most of these patients can be explained by the regular attendance at the public healthcare network, represented by an approximate annual average of three consultations, as well as the supply of the main medications by the public healthcare system.

Due to the possibility of diagnosis still in the neonatal period[1], the average age at diagnosis for these patients can be considered high (2 years), but it was lower than the national average, which showed an age at diagnosis of almost 6 years[17]. Even so, less than half of the individuals obtained their diagnosis through the NST. In Brazil[17], from 2009 to 2017, 2,441 cases of cystic fibrosis were diagnosed, of which 49.7% were diagnosed by neonatal screening. In the years 2016 and 2017, neonatal screening was already responsible for more than 60% of new diagnoses, being, therefore, lower than the national percentage.

There is evidence that patients diagnosed with CF from the NST benefit from early intervention, starting earlier follow-up with drug and nutritional treatment, in addition to follow-up with pulmonary function tests[5]. In the same study, Lumertz et al.[5] found better values of the Shwachman score, with statistical significance, and a tendency to higher means of the Z score for BMI in patients diagnosed by the NST.

Most of these patients (20/87%) already had manifestations of the disease at the time of diagnosis, the most frequent being persistent respiratory symptoms and growth deficits or malnutrition, as also observed by the GBEFC[17]. These manifestations are explained by CFTR deregulation, intraluminal secretions become dense and increased mucus production causes obstruction and inflammation in the organs, causing symptoms[19].

As in the study by Rosa et al.[20], there was a statistically significant predominance of homozygous individuals. These individuals usually have early respiratory symptoms, decreased lung function, pancreatic insufficiency, and growth retardation.

Because this is a multisystemic disease, there was a diverse pharmacotherapeutic prescription, with an average of four continuous medications being used, a lower number than that found in another study[18], in which they found an average use of 6.5 medication/patient. In the same study, dietary and metabolic therapy was described as the main treatment requirement, followed by drugs for respiratory disorders, as was evidenced in the patients in the study, who used mainly pancreatin, multivitamins and dornase alfa, supported by the main symptoms of CF[19]. In Brazil[17], dornase alfa is prescribed to more than 70% of patients, as there is evidence that its use reduces the risk of death, improves lung function and reduces exacerbations[21].

Pulmonary exacerbations occurred in almost half of the individuals with CF, the same reported by the GBEFC[17], in which 49.3% had at least one exacerbation in 2017. A retrospective and documentary study[22] showed that respiratory causes were the main responsible for hospitalizations and the most frequent clinical manifestation was persistent cough and recurrent hospitalizations for bronchiectasis, pancreatic insufficiency and pneumonia.

The Shwachman score[11], published by him together with Kulczcki in 1958, serves as an estimate of the evolution of the disease, which covers the following domains: general activity, nutrition, radiological examination and physical assessment. Each cited area is scored between five and 25 points, the score being stratified and considered severe when the sum is equal to or less than 40 points and as excellent when it has 86 or more points. Lumertz et al.[5] emphasized that this score is an assessment clinical-radiological technique established and used not only in services that monitor patients with CF, but also as a measure of research outcome.

The assessment of severity using the Shwachman-Kulczycki Score revealed a mean score of 78.5±16.7; most of which were classified as Good or Excellent, similar to that found in other studies[10,14] which also described good clinical conditions in this series, with a mean of 81.8±14.2 and 86.9±17.9, respectively. In Brazil, the majority of patients aged up to 15 years had a mean Shwachman-Kulczycki Score classified as Good and Excellent, but with a tendency to reduce the score with age[15,17], since there are increased nutritional needs due to growth and more frequent lung infections in older age groups[14]. These good clinical conditions can be explained by the regular follow-up and because they are mostly infants, preschoolers and schoolchildren, who are eutrophic, as stated in other studies[14,15]. Adde[23] noticed that nutritional management contributed significantly to the reduction of progressive rates of CF, related to the deterioration of lung function, improving the quality of life of patients. However, when these individuals were evaluated according to the presence of nutritional deficit established by the value of any Z-Score<-1, similar values were found by other studies[14,15], with almost 70% presenting such deficiency.

The nutritional care guideline for children and adults with CF published by Turck et al.[16] showed that the anthropometric criteria most regularly used to assess nutritional status in this group of patients, as they are associated with lung function and survival, are indicators weight-for-height (W/H) and body mass index-for-age (BMI/A). Currently, it is recommended that children and adolescents with CF should maintain their BMI/A ≥ 50th percentile. The CF Patient Registry Report[6] still reports that 45.3% of children did not reach the nutritional parameters required for treatment[16]. Hauschild et al.[10] also found that 65.8% of the patients studied had a percentile <50, although this fact was not associated with impaired pulmonary function. In the present research, it was reported that, despite the majority being eutrophic, more than 80% were outside the nutritional recommendations[16], a statistically significant number and higher than the national data[6]. Repeated respiratory infections associated with chronic inflammation and malabsorption trigger a nutritional deficit, interfering with pulmonary prognosis. The loss of muscle mass and, consequently, the reduction of strength and resistance of the respiratory muscles, compromises diaphragm function. Impaired pulmonary function favors recurrent infections, which increases energy demand, triggering a worsening of the pulmonary condition[4].

In the study by Pinto, Silva and Britto[14], the mean Shwachman-Kulczycki score was significantly higher in individuals without nutritional deficit, without statistical significance for the other socioeconomic and clinical variables, as in this study. This data corroborates the influence of nutritional status in determining this severity index. Another study that evaluated the nutritional status of patients with CF[15] also did not show an association between nutritional status and family income, despite a description of worsening of nutritional status in patients with unfavorable economic conditions[14]. Although there was no significance between the other clinical and socioeconomic variables investigated, to the detriment of nutritional status, this measurement is important to estimate the prognosis of patients, since, according to a study by Hauschild et al.[10], which evaluated the correlation of the nutritional status with lung function, patients classified as having nutritional failure showed a relative risk of 5.00 for impaired lung function after 36 months of the study. Those classified below the 50th percentile had a relative risk of 4.61 for the outcome. This study[10] concluded that nutritional status was correlated

with impaired pulmonary function, with nutritional status being the determining risk factor in the respiratory quality of patients with CF. Estimating nutritional losses in patients with CF over the course of the disease is the main strategy to avoid complications. Measures for recovery and maintenance of nutritional status should be introduced early[9,10].

Most individuals with nutritional deficit were not diagnosed early using the NST, despite having a lower mean age at diagnosis – revealing the fact that they had earlier manifestations of the disease, which allowed clinical diagnosis, and, consequently, generated earlier impairment of the nutritional status. The opposite was observed by Pinto, Silva and Britto[14], in which patients with nutritional deficit presented a higher age at diagnosis than those without nutritional deficit, which may be explained by a later onset of therapy.

CONCLUSION

Pediatric patients with CF followed up in Piauí have socioeconomic, clinical and nutritional characteristics, for the most part, similar to national data. Despite the limitation of the study, due to the small sample, we found that maternal aspects did not influence the nutritional status of these individuals, as well as other socioeconomic characteristics. There was a delay in diagnosis, as well as low coverage for performing NST for the diagnosis of CF. Despite this, they underwent regular follow-up with the use of food, metabolic and respiratory therapy, which provided a satisfactory nutritional status, although most of them did not reach the nutritional recommendation for adequate management of the disease. Nutritional status influenced the severity score of individuals, confirming the importance of adequate management and nutritional monitoring to improve the pulmonary prognosis and quality of life of these patients.

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